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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/316,387	05/21/1999	ALAN SOLOMON	UNIE-014/01US 306680-2015	7724

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EXAMINER	
BALLARD, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
1649	

MAIL DATE	DELIVERY MODE
09/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/316,387	SOLOMON ET AL.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,28 and 30-49* is/are pending in the application.

4a) Of the above claim(s) *28 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,30-35 and 37-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 8, 2007 has been entered.

The Examiner of U.S. Patent Application No. 09/316,387 has changed. In order to expedite the correlation of papers with the application, please direct all future correspondence to Examiner Ballard, Technology Center 1600, Art Unit 1649.

Status of Application, Amendments and/or Claims

Claims 24, 28 and 30-49 are pending in the current application.

Claims 28 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 4, 2002.

Accordingly, claims **24, 30-35** and **37-49** are under examination in the current Office action.

Election/Restrictions

In the response filed June 8, 2007, Applicants request that claims 28 and 36 be rejoined with the elected claims currently under examination. Applicants submit that the originally elected species of "immunoglobulin reactive with a non-light chain amyloid" as the functional species encompasses antibodies raised against Ig light chains and/or reactive with Ig light chains, because these antibodies also react with β-amyloid. Thus, withdrawn claims 28 and 36 are encompassed by the elected species.

Applicants' arguments are the same as previously presented, and thus have already been considered and addressed in the previous Office action (05/09/2006). In particular, the fact that a specific antibody generated with specificity to light chain amyloid cross-reacts with β-amyloid does not evidence that the opposite is true, i.e., that an antibody generated with specificity to β-amyloid will necessarily react with light chain amyloid. Antibodies that bind to non-light chain amyloids (such as β-amyloid) are a genus that is non-coextensive with antibodies that bind to light chain amyloids, i.e., the species and/or subgenus are not of the same scope. A search for antibodies that opsonize and/or react with non-light chain amyloid is not the same as, nor co-extensive with, a search for antibodies generated to light chain amyloids. Accordingly, the restriction is proper and withdrawal of the non-elected invention is maintained, as noted in the previous Office action, which made the restriction requirement FINAL.

Response to Amendment

Upon further consideration and as discussed in the interview with Applicants' representatives on October 30, 2006, the declaration filed on March 6, 2006 under 37 CFR 1.131 is sufficient to overcome the Schenk references (US patents 6,787,523 and 6,743,427).

Withdrawn Claim Rejections

The rejection of claims 24, 30-35 and 37-49 under 35 USC 102(e) (Schenk patents), as set forth in previous Office actions, is withdrawn in view of the reconsidered declaration under 37 CFR 1.131 as noted above.

The rejection of claims 24, 30-35 and 37-49 under 35 USC 103(a), as set forth in previous Office actions and which utilized the above Schenk references (US patents 6,787,523 and 6,743,427) for support, is withdrawn in view of the reconsidered declaration under 37 CFR 1.131 as noted above.

Maintained Claim Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 24, 30-31, 35 39-46 and 48-49 under 35 U.S.C. 102(b) as being anticipated by Konig et al. (WO 96/25435) is maintained for reasons of record.

In the response filed June 8, 2007, Applicants argue that the Konig et al. does not teach each and every limitation of the claimed invention. In particular, Applicants note that the prevention of aggregation of amyloid plaques disclosed in Konig is different from removing a previously formed plaque. Applicants also submit that there was no actual administration of the antibodies performed or described in the patent publication. Moreover, Applicants argue that the C-terminal antibody disclosed by Konig would not be effective to reduce plaque burden, because as evidenced by the Schenk '427 patent (previously cited as above), not all C-terminal antibodies can have an effect on plaque burden. Therefore, Applicants assert that Konig does not anticipate, directly or inherently, the current claims. Applicants thus argue that Konig fails to teach the two elements of an amount of antibody "effective to remove amyloid deposits" and "removal of amyloid" required by the instant claims.

Applicant's arguments filed June 8, 2007 have been fully considered but they are not persuasive. Applicants' arguments are essentially the same as presented in previous responses, and thus the rejection is maintained for the same reasons of record. Konig et al. teach the use of specific antibodies in methods of treatment for Alzheimer's disease, wherein the treatment includes the extraction of β-amyloid species (see in particular p. 25, lines 14-18). Konig teaches the therapeutic administration of

the antibodies in pharmaceutical formulations to Alzheimer's patients (see p. 7, lines 21-23, p. 14, lines 8-11, and p. 25, lines 14-18), which anticipates the method step of the claims. It is true that Konig does not teach the definitive mechanism for the treatment provided to Alzheimer's patients via administration of anti-β-amyloid antibodies. However, the mechanism of the treatment is not required for Konig to be anticipatory or enabling, as it is inherent to the method step taught by Konig. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). And also MPEP § 2121, which notes that:

> When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

Applicant has provided no facts that the antibody of Konig fails to work via opsonization. Only assertions are provided. The fact that Schenk notes that the C-terminal antibody 16C11 fails to affect amyloid plaque burden is therefore also irrelevant to the instant case, because it is a completely different antibody than the monoclonal 369.2B antibody disclosed by Konig. There is no teaching in the art, nor any factual evidence brought forth on the record, that the 369.2B mAb would not be capable of removing amyloid deposits. Additionally, the fact that certain antibodies noted in other prior art fail to elicit the desired removal of amyloid would in fact call into question the enablement of the

broadly claimed current method, as the instant claims do not recite *any* specific antibody epitope and thus encompass *any* antibody or immunoglobulin polypeptide.

Moreover, Konig teaches that the 369.2B mAb binds to diffuse amyloid, fibrillar amyloid, vascular amyloid and neurofibrillary tangles (see p. 6, lines 23-25). It is noted at page 5, lines 1-3 of the instant specification that "[U]pon the binding or adhering of such immunoglobulin polypeptides to undesired deposits of amyloid fibrils, the latter are believed to be oponized." And at page 12, lines 1-5, the instant specification defines "opsonize" as "the binding of an immunoglobulin polypeptide to a particular target, particularly epitopes found on deposits of amyloid fibrils, such that the antibody and targets together are recognized as "foreign" by the host's cellular immune system. In other words the binding of the immunoglobulin of the present invention enhances the phagocytization of the amyloid fibrils." Thus, as defined by Applicants' own disclosure, there would be no mechanistic difference between administration of the β-amyloid specific monoclonal antibody disclosed by Konig and the instantly claimed antibodies, as the binding of these antibodies to amyloid fibrils would in both cases be expected to inherently enhance the opsonization of amyloid fibrils as mediated by the patient's own immune system. A prior art reference is not required to teach the mechanism of action in order to meet the requirements of either anticipation or enablement. As both Konig's therapeutic method and the currently claimed method provide for the administration of the same antibodies to the same patient population for the same purpose, the mechanism of removal of amyloid deposits would be inherently expected. It is thus

Applicants' burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicants' claims.

Finally, with respect to Applicants' argument that Konig et al. does not teach "an amount effective to remove amyloid deposits", the reference clearly teaches the requirement for the antibody to bind the β-amyloid antigen. Such binding would be expected to elicit Konig's disclosed method of extracting the aggregated β-amyloid deposits following administration of the antibody for therapeutic purposes, such as for treatment of Alzheimer's disease (AD). The skilled artisan would recognize that regardless the desired mechanism of action of the antibody, the end goal of administration of the antibody is to elicit a therapeutic response, and thus in treatment of AD, the amount administered to the patient would in fact have to be an effective amount. Moreover, the instant claims are not limited to any specific quantity and the instant specification indicates that the only requirement is that antibody/antigen binding occurs. Accordingly, Konig is on point to the same dosage requirement as instant claimed and the case law noted is supportive to the teachings which are literally and inherently provided. Therefore, the rejection of claims 24, 30-31, 35 39-46 and 48-49 is maintained.

The rejection of claims 24, 30-35 and 37-49 under 35 U.S.C. 102(b) as being anticipated by Becker (Nettleship) et al. (EP 613007) is maintained for reasons of record.

In the response filed June 8, 2007, Applicants argue that Becker et al. fails to provide any discussion of the amount of antibody that is to be administered to a patient to remove amyloid deposits, nor does Becker disclose or show removal of amyloid deposits as claimed. Moreover, Applicants submit that Becker dose not provide an enabling disclosure for administering to the patient and antibody or immunoglobulin polypeptide or fragment thereof in an amount effective to remove amyloid deposits.

Applicant's arguments filed June 8, 2007 have been fully considered but they are not persuasive. Applicants' arguments are essentially the same as presented in previous responses, and thus the rejection is maintained for the same reasons of record. As stated previously, the question of anticipation here is whether or not the methods are the same or different. Applicants' claims are directed to a method of removing amyloid deposits in a patient comprising administering an antibody or immunoglobulin polypeptide that opsonizes an amyloid fibril and induces removal of amyloid deposits. Alzheimer's disease is a neurodegenerative disorder characterized by the abnormal deposition of protein aggregates composed of neurofibrillary tangles and amyloid plaque cores (see Becker, column 1, lines 1-10). Becker also teaches that β-amyloid protein that adopts a β-sheet conformation (which conformation is known to form amyloid fibrils and subsequently aggregate into amyloid deposits) is particularly neurotoxic to neurons, and teaches that antibodies specific for β-amyloid peptides of the β-sheet conformation are useful for inhibiting the neurotoxicity of these peptides (see column 5, lines 27-50). Becker additionally teaches the therapeutic use of such antibodies for the treatment of human patients with Alzheimer's disease (column 7, 39-

52). The instant claims evidence that the claimed antibodies are reactive with Alzheimer's Aβ protein (claim 41). Thus it can be seen that both Becker's therapeutic method and the currently claimed method provide for the administration of the same antibodies to the same patient population for the same purpose.

Becker specifically states that "therapeutics" means "treatment...of disease states or biological status via the *in vivo* administration to mammals, preferably humans, of the antibodies of the present invention" (column 7, lines 44-49). One of skill in the art would immediately recognize that such would mean administration of the antibody in an amount sufficient to elicit an effective (i.e., therapeutic) response. And as noted previously, it is well within the skill of the artisan to determine administrable amounts of the antibody sufficient to effect the desired response of binding to β-amyloid, inhibiting neurotoxicity and thus providing treatment.

Moreover, it is noted at page 5, lines 1-3 of the instant specification that "[U]pon the binding or adhering of such immunoglobulin polypeptides to undesired deposits of amyloid fibrils, the latter are believed to be oponized." And at page 12, lines 1-5, the instant specification defines "opsonize" as "the binding of an immunoglobulin polypeptide to a particular target, particularly epitopes found on deposits of amyloid fibrils, such that the antibody and targets together are recognized as "foreign" by the host's cellular immune system. In other words the binding of the immunoglobulin of the present invention enhances the phagocytization of the amyloid fibrils." Thus, as defined by Applicants' own disclosure, there would be no mechanistic difference between administration of the β-amyloid specific antibodies disclosed by Becker and the instantly

claimed antibodies, as the binding of these antibodies to amyloid fibrils would in both cases be expected to inherently enhance the opsonization of amyloid fibrils as mediated by the patient's own immune system. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Thus, while the exact mechanism by which Becker's disclosed antibodies work to reduce neurotoxicity and thereby treat a patient having Alzheimer's disease may not have been fully appreciated by Becker, administration of the antibodies for therapeutic purposes would nonetheless inherently result in the opsonization of amyloid deposits as currently claimed.

With regard to Applicants' argument that the Becker reference is non-enabling, MPEP § 2121 notes that:

> When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

Thus, it is Applicants' burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicants' claims. Reasons showing inherency have clearly been shown, both here and of record, and there are no structural limitations to the immunoglobulin polypeptides (antibodies), their amounts or administration that teach over the prior art reference. There is no

precedent in the cited case law to conclude that Becker is non-enabled. As noted previously, the above appears to be more a question of fact to which Applicants have shown no evidence or scientific reasoning that would disprove the teachings of Becker, and thus Applicants' questioning of Becker's enablement reflects upon the enablement of the instant claims, as the Becker teachings are not differentiated therefrom. Accordingly, the rejection of claims 24, 30-35 and 37-49 as anticipated by Becker et al. is maintained.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
August 29, 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646